

Application Serial No. 09/937,899  
Amendment Dated XX September 2004  
Reply to Office Action of 30 June 2004

*AMENDMENTS TO THE SPECIFICATION*

Please amend the following paragraphs found on page 4 of the specification. These paragraphs were originally submitted in the Amendment dated 15 April 2004.

Figure 2 shows the predicted secondary structure of preproNPY mRNA and the predicted structure of the 5' end (1 to 138 bases) of the full preproNPY mRNA sequence published in GenBank Accession No. K01911. The secondary structure was predicted by using the MFOLD program of the Genetics Computer Group of the University of Wisconsin. Squiggle plot of: osa1.mfold February 7, 19100 12:46. (Linear) MFOLD of: osa1.seqT: 37.0 Check: 5173 from: 1 to: 138 February 7, 19100 12:43. Length 138 Energy -28.4. The nucleotide sequence “acaagcgacugg” is the wildtype sequence of SEQ ID NO:7.

Figure 3 shows the predicted secondary structure of mutated preproNPY mRNA and the predicted structure of the 5' end (1 to 138 bases) of the full mutated preproNPY mRNA sequence published in GenBank Accession No. K01911. The secondary structure was predicted by using the MFOLD program of the Genetics Computer Group of the University of Wisconsin. The mutated base T to C is base number 106. Squiggle plot of: osa2.mfold February 7, 19100 14:11. (Linear) MFOLD of: osa2.seqT: 37.0 Check: 4340 from: 1 to: 138 February 7, 19100 14:07. Length 138 Energy -26.4 -28.4. The nucleotide sequence “acaagcgaccgg” is the mutant sequence of SEQ ID NO:7.

Please amend the first paragraph on page 8 to read as follows.

We are counteracting the influence of the mutated NPY gene by using a short, allele specific oligonucleotide, which includes the sequence of the mutated part: ... cga ct/cg ggg ... (mutated based

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marked on bold) (SEQ ID NO:8). This can be accomplished by using oligonucleotides of various lengths, but all recognizing the mutated base sequence. According to the predicted secondary structure of preproNPY mRNAs (Fig 1 and 2 Figs. 2 and 3), the best target sequence is between -9 and +2 bases around the mutation, i.e., a sequence targeting to 3'-ac aag cga ctg g-5' 5'-ac aag cga ccg g-3' (SEQ ID NO:9). This sequence contains 'bulbs' which are known to enhance the binding of oligonucleotide to the target mRNA.